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=> s glycoconjugate
L1       30715 GLYCOCONJUGATE

=> s l1 and antibod?
L2        5040 L1 AND ANTIBOD?

=> s l2 and toxin
L3         217 L2 AND TOXIN

=> s l3 and carbohydrate linkage
L4           0 L3 AND CARBOHYDRATE LINKAGE

=> s l3 and polyethylene glycol
L5           4 L3 AND POLYETHYLENE GLYCOL

=> dup remove l5
PROCESSING COMPLETED FOR L5
L6           4 DUP REMOVE L5 (0 DUPLICATES REMOVED)

=> d l6 1-4 cbib abs

L6   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:122585   Document No. 142:217398  Cell-free in vitro glycoconjugation of
     interleukin 2 as therapeutic agent against cancer and AIDS in mammal and
     human.  Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes,
     David; Chen, Xi (Neose Technologies, Inc., USA).  U.S. Pat. Appl. Publ. US
     20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779.
     (English).  CODEN: USXXCO.  APPLICATION: US 2003-410980 20030409.
     PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US
     2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607;
     US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P
     20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US
     2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB   The invention includes methods and compns. for remodeling a peptide mol.,
     including the addition or deletion of one or more glycosyl groups to a
     peptide, and/or the addition of a modifying group to a peptide.  The method
     uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester
     group-containing saccharide to interleukin 2 peptide, and then conjugate the
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saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

2004:267260 Document No. 140:297533 Peptides and related molecules that modulate nerve growth factor activity. Boone, Thomas C.; Wild, Kenneth D., Jr.; Sitney, Karen C.; Min, Hosung; Kimmel, Bruce (Amgen Inc., USA). PCT Int. Appl. WO 2004026329 A1 20040401, 267 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US29866 20030919. PRIORITY: US 2002-412524P 20020919; US 2003-666480 20030918.

AB The present invention relates to certain biol. active peptides and polypeptides which can be used as therapeutics or prophylactics against diseases or disorders linked to nerve growth factor (NGF) as the causative agent. In one aspect of the present invention, pharmacol. active polypeptides comprising peptides linked to one or more Fc domains are provided.

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.

AB The invention includes methods and comps. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or

GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

2003:301098 Document No. 138:316492 Glycan remodeling and glycoconjugation of peptides and proteins. De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2003031464 A2 20030417, 900 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US32263 20021009. PRIORITY: US 2001-344692P 20011019; US 2001-334233P 20011128; US 2001-334301P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828.

AB The invention includes methods and compns. for the cell-free in vitro addition and/or deletion of sugars to or from a peptide mol. in such a manner as to provide a glycopeptide mol. having a specific customized or desired glycosylation pattern, wherein the glycopeptide is produced at an industrial scale. The glycopeptide so produced may have attached thereto a modified sugar that has been added to the peptide via an enzymic reaction. A key feature of the invention is to take a peptide produced by an cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a glycopeptide having a glycosylation pattern suitable for therapeutic use in a mammal. More specifically, it is possible to prepare a glycopeptide mol. having a modified sugar mol. or other compound conjugated thereto, such that the conjugated mol. confers a beneficial property on the peptide. The conjugate mol. is added to the peptide enzymically because enzyme-based addition of conjugate mols. to peptides has the advantage of regioselectivity and stereoselectivity. It is therefore possible to remodel a peptide by confering upon the peptide a desired glycan structure preferably having a modified sugar attached thereto, and to generate the glycopeptides at an industrial scale. The invention thus provides a practical solution for the efficient production of improved therapeutic peptides.

=> s l3 and glycosyl linking group
L7 0 L3 AND GLYCOSYL LINKING GROUP

=> s glycosyl linker

```
L8            0 GLYCOSYL LINKER

=> s l3 adn polyamine
MISSING OPERATOR L3 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l3 and polyamine
L9            2 L3 AND POLYAMINE

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10           2 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> d l10 1-2 cbib abs

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
2006:273970   Document No. 144:307924  Multi-chromophoric quencher constructs
      for use in high sensitivity energy transfer probes.  Benson, Scott C.;
      Menchen, Steven M.; Upadhya, Krishna G. (Applera Corporation, USA).  PCT
      Int. Appl. WO 2006031851 A1 20060323, 61 pp.  DESIGNATED STATES: W:  AE,
      AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR,
      CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU,
      ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
      MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT,
      RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
      US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,
      CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL,
      PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO
      2005-US32659 20050914.  PRIORITY: US 2004-609273P 20040914.
AB    Dark quencher constructs, termed "multi-chromophoric quenchers" are
      described herein that comprise at least two dark quenching moieties, which
      can be the same or different, linked together by at least one multivalent
      linking moiety.  The structure of the multi-chromophoric quenchers can be
      varied to selectively enhance quenching within a specific range of
      reporter emission wavelengths.  This can be accomplished by linking
      together, into a single mol., two or more identical quenchers, by reacting
      the quenchers with a multivalent linker.  The structure of the
      multi-chromophoric quencher can also be varied to quench a broader range
      of reporter emission wavelengths than previously possible.  This can be
      accomplished by linking together, into a single mol., two or more
      different quenchers, by reacting the quenchers with a multivalent linker.
      The structure of the multi-chromophoric quencher can also be varied to
      simultaneously broaden the absorption range and increase the total
      absorption within the absorption range.  This can be done by combining the
      two concepts described above.  In other words, multiple types of quenching
      moieties can be employed to increase the absorption range and a multiple
      number of each type of quenching moiety can be used to increase the total
      absorptivity within the absorption range.  The multi-chromophoric
      quenchers can be tethered to probes for biomols., insol. supports and/or
      fluorescent dyes for use in a wide variety of biomol. assays.  N,N'-bis
      dabsyl-ornithine NHS ester, prepared from L-ornithine Me ester and dabsyl
      NHS, was conjugated to a 5'-derivatized 3'-FAM oligonucleotide to prepare a
      multi-chromophoric quencher construct.

L10  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
2003:133942   Document No. 138:149630  Dye-sulfenates for dual phototherapy.
      Rajagopalan, Raghavan; Achilefu, Samuel I.; Bugaj, Joseph E.; Dorshow,
      Richard B. (Mallinckrodt Inc., USA).  U.S. Pat. Appl. Publ. US 20030036538
      A1 20030220, 11 pp., Cont.-in-part of U.S. Ser. No. 484,322.  (English).
      CODEN: USXXCO.  APPLICATION: US 2001-898809 20010703.  PRIORITY: US
      2000-484322 20000118.
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AB The present invention discloses dye-sulfenate derivs. and their bioconjugates for dual phototherapy of tumors and other lesions. The compds. of the present invention may contain either a mixture of Type 1 and Type 2 agents or a single entity that integrates both units in the same mols. The compds. are designed to produce both Type 1 and Type 2 phototherapeutic effect at once using dual wavelength light source that will produce singlet oxygen and free radicals at the lesion of interest.

=> s dendrimer
L11 28339 DENDRIMER

=> s l11 and antibod?
L12 799 L11 AND ANTIBOD?

=> s l12 and glycosylated
L13 2 L12 AND GLYCOSYLATED

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14 2 DUP REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-2 cbib abs

L14 ANSWER 1 OF 2 MEDLINE on STN
2008175312. PubMed ID: 18310320. Targeting the carbohydrates on HIV-1: Interaction of oligomannose dendrons with human monoclonal antibody 2G12 and DC-SIGN. Wang Sheng-Kai; Liang Pi-Hui; Astronomo Rena D; Hsu Tsui-Ling; Hsieh Shie-Liang; Burton Dennis R; Wong Chi-Huey. (Departments of Chemistry and Immunology and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA. ) Proceedings of the National Academy of Sciences of the United States of America, (2008 Mar 11) Vol. 105, No. 10, pp. 3690-5. Electronic Publication: 2008-02-29. Journal code: 7505876. E-ISSN: 1091-6490. Pub. country: United States. Language: English.

AB It is widely accepted that the heavily glycosylated glycoprotein gp120 on the surface of HIV-1 shields peptide epitopes from recognition by the immune system and may promote infection in vivo by interaction with dendritic cells and transport to tissue rich in CD4(+) T cells such as lymph nodes. A conserved cluster of oligomannose glycans on gp120 has been identified as the epitope recognized by the broadly HIV-1-neutralizing monoclonal antibody 2G12. Oligomannose glycans are also the ligands for DC-SIGN, a C-type lectin found on the surface of dendritic cells. Multivalency is fundamental for carbohydrate-protein interactions, and mimicking of the high glycan density on the virus surface has become essential for designing carbohydrate-based HIV vaccines and antiviral agents. We report an efficient synthesis of oligomannose dendrons, which display multivalent oligomannoses in high density, and characterize their interaction with 2G12 and DC-SIGN by a glycan microarray binding assay. The solution and the surface binding analysis of 2G12 to a prototype oligomannose dendron clearly demonstrated the efficacy of dendrimeric display. We further showed that these glycodendrons inhibit the binding of gp120 to 2G12 and recombinant dimeric DC-SIGN with IC(50) in the nanomolar range. A second-generation Man(9) dendron was identified as a potential immunogen for HIV vaccine development and as a potential antiviral agent.

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
2005:158490 Document No. 142:235999 Biosensors utilizing dendrimer -immobilized ligands and their use thereof. Spangler, Brenda D.; Spangler, Charles W. (Montana State University, USA). PCT Int. Appl. WO 2005016115 A2 20050224, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,

AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1961 20040123. PRIORITY: US 2003-442270P 20030123.

AB The present invention is directed to methods and compns. useful as biosensors that specifically interact with various pathogens and other target analytes. The biosensor itself comprises functionalized dendritic tethers derivatized for attachment to a variety of surfaces as self-assembled monolayers (SAMs) as well as attached binding moieties (sometimes referred to as capture binding ligands). Accordingly, the present invention provides compns. comprising supports comprising surfaces to which the binding moieties (e.g. antibodies) are attached for the detection of target analytes (e.g. pathogens) as well as methods and compns. relating to the attachment of such binding moieties.

=> s l2 and polyethylene glycol
L15 34 L2 AND POLYETHYLENE GLYCOL

=> s l15 and toxin
L16 4 L15 AND TOXIN

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17 4 DUP REMOVE L16 (0 DUPLICATES REMOVED)

=> d l17 1-4 cbib abs

L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine,

UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L17 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
2004:267260 Document No. 140:297533 Peptides and related molecules that modulate nerve growth factor activity. Boone, Thomas C.; Wild, Kenneth D., Jr.; Sitney, Karen C.; Min, Hosung; Kimmel, Bruce (Amgen Inc., USA). PCT Int. Appl. WO 2004026329 A1 20040401, 267 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US29866 20030919. PRIORITY: US 2002-412524P 20020919; US 2003-666480 20030918.
AB The present invention relates to certain biol. active peptides and polypeptides which can be used as therapeutics or prophylactics against diseases or disorders linked to nerve growth factor (NGF) as the causative agent. In one aspect of the present invention, pharmacol. active polypeptides comprising peptides linked to one or more Fc domains are provided.

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that

the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

L17 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
2003:301098 Document No. 138:316492 Glycan remodeling and glycoconjugation of peptides and proteins. De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2003031464 A2 20030417, 900 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US32263 20021009. PRIORITY: US 2001-344692P 20011019; US 2001-334233P 20011128; US 2001-334301P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828.
AB The invention includes methods and compns. for the cell-free in vitro addition and/or deletion of sugars to or from a peptide mol. in such a manner as to provide a glycopeptide mol. having a specific customized or desired glycosylation pattern, wherein the glycopeptide is produced at an industrial scale. The glycopeptide so produced may have attached thereto a modified sugar that has been added to the peptide via an enzymic reaction. A key feature of the invention is to take a peptide produced by an cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a glycopeptide having a glycosylation pattern suitable for therapeutic use in a mammal. More specifically, it is possible to prepare a glycopeptide mol. having a modified sugar mol. or other compound conjugated thereto, such that the conjugated mol. confers a beneficial property on the peptide. The conjugate mol. is added to the peptide enzymically because enzyme-based addition of conjugate mols. to peptides has the advantage of regioselectivity and stereoselectivity. It is therefore possible to remodel a peptide by confering upon the peptide a desired glycan structure preferably having a modified sugar attached thereto, and to generate the glycopeptides at an industrial scale. The invention thus provides a practical solution for the efficient production of improved therapeutic peptides.

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L19 ANSWER 1 OF 18 MEDLINE on STN
2003303535. PubMed ID: 12832795. Crystallization and preliminary X-ray analysis of an anti-LewisX Fab fragment with and without its LewisX antigen. van Roon Anne-Marie M; Pannu Navraj S; Hokke Cornelis H; Deelder Andre M; Abrahams Jan Pieter. (Biophysical Structural Chemistry, Leiden University, Einsteinweg 55, 2333 CC Leiden, The Netherlands. ) Acta

crystallographica. Section D, Biological crystallography, (2003 Jul) Vol. 59, No. Pt 7, pp. 1306-9. Electronic Publication: 2003-06-27. Journal code: 9305878. ISSN: 0907-4449. Pub. country: Denmark. Language: English.

AB LewisX-containing glycoconjugates are abundantly expressed by schistosomes and are assumed to be of prime importance for the survival of the parasite within the human host. Monoclonal antibody 291-2G3-A, which was generated from mice infected with schistosomes, was found to interact with monomers, dimers and trimers of the LewisX trisaccharide. The Fab fragment of monoclonal antibody 291-2G3-A has been crystallized and soaked with its LewisX antigen. X-ray data sets were recorded for the different Fab crystals with and without LewisX. Crystals grown from 25% polyethylene glycol 3350, 0.17 M ammonium sulfate and 15% glycerol belong to the triclinic space group P1, with unit-cell parameters a = 67.4, b = 71.6, c = 104.8 A, alpha = 86.5, beta = 71.3, gamma = 83.3 degrees for the native crystals and with slightly different unit-cell parameters a = 67.3, b = 72.4, c = 104.8 A, alpha = 85.8, beta = 71.3, gamma = 83.3 degrees for the crystals containing bound LewisX. Crystals grown from 14% PEG 3350, 50 mM Tris pH 8 and soaked with LewisX also belong to the triclinic space group P1, but with different unit-cell parameters a = 45.1, b = 60.8, c = 91.6 A, alpha = 96.0, beta = 95.4, gamma = 101.8 degrees.

L19 ANSWER 2 OF 18 MEDLINE on STN

2002271013. PubMed ID: 12009948. Evaluation of different alpha-Galactosyl glycoconjugates for use in xenotransplantation. Byrne Guerard W; Schwarz Alexander; Fesi Joanna R; Birch Patrick; Nepomich Anna; Bakaj Ivona; Velardo Margaret A; Jiang Cong; Manzi Adriana; Dintzis Howard; Diamond Lisa E; Logan John S. (Nextran Inc., 303B College Road, Princeton, New Jersey, USA.. gbyrne@nextran.com) . Bioconjugate chemistry, (2002 May-Jun) Vol. 13, No. 3, pp. 571-81. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB Porcine organs are rapidly rejected after transplantation into primate recipients due to the presence of preexisting immunoglobulins that bind to terminal galactose alpha1,3 galactose residues (alpha-galactosyl) present on porcine glycoproteins and glycolipids. Currently available immunosuppressive reagents have been largely ineffective at controlling the synthesis of these anti-Gal antibodies. Nonantigenic hapten polymers have been shown to be effective materials for blocking humoral immune responses in various model systems. We have developed a series of alpha-galactosyl glycoconjugate polymers and tested their ability to block anti-Gal antibody binding in vitro and in vivo. A galactose alpha1,3 galactose beta 1,4 GlcNAc trisaccharide free acid (TRFA) with a hexanoic acid spacer, containing five methylene groups and a carboxylic acid, was produced and coupled to a variety of polymeric backbones including dextran, branched poly(ethylene glycol) (PEG), and poly-L-lysine. The ability of monomeric TRFA and the alpha-galactosyl conjugates to block anti-Gal IgG and IgM binding was determined using a competition ELISA assay on defined HSA-Gal glycoconjugates and porcine microvascular endothelial cell substrates. We show that branched PEG carriers, with a TRFA sugar attached to each branch, exhibit enhanced antibody blocking ability compared to TRFA, but at higher target antigen densities these simple PEG conjugates are no more effective then an equivalent amount of TRFA in blocking anti-Gal IgM antibody interactions. In contrast, polymers of the branched PEG conjugates and linear conjugates made using dextran and poly-L-lysine were 2000 to 70000-fold more effective inhibitors of anti-Gal antibodies. In a study using nonhuman primates, a single dose infusion of polymeric PEG or dextran glycoconjugates dramatically reduced the level of circulating anti-Gal antibodies in cynomologus monkeys for at least 72 h. Glycoconjugates similar to these might be useful both to block anti-Gal interactions in vivo and to specifically control

the induced anti-Gal immune response.

L19 ANSWER 3 OF 18 MEDLINE on STN
1999285841. PubMed ID: 10359308. Isolation and partial characterisation of the Triton X-100 solubilised protein antigen from Mycobacterium tuberculosis. Kim H J; Jo E K; Park J K; Lim J H; Min D; Paik T H. (Department of Microbiology, College of Medicine, Chungnam National University, Taejeon, Republic of Korea. ) Journal of medical microbiology, (1999 Jun) Vol. 48, No. 6, pp. 585-91. Journal code: 0224131. ISSN: 0022-2615. Pub. country: ENGLAND: United Kingdom. Language: English.
AB This report describes extraction of a new native antigen fraction from Mycobacterium tuberculosis without massive degradation of proteins by Triton X-100. The Triton X-100 solubilised protein (TSP) antigen showed a characteristic antigen profile and reproducible extraction pattern. To characterise the nature of their composition, the TSP antigen was fractionated by Triton X-114 phase partitioning. The TSP antigen contained a variety of lipids and glycoconjugates as well as diverse proteins. Most proteins were partitioned into the aqueous phase during phase fractionation, whereas non-protein molecules and lipoproteins were recovered in the detergent phase. The lymphoproliferative responses to the TSP aqueous fraction in healthy tuberculin reactors were significantly higher than those to the purified protein derivative (PPD) and unfractionated TSP. In contrast, the antibody responses to TSP aqueous fraction in tuberculosis patients showed weak reactivity. This study suggests that the TSP aqueous fraction can be used as a T-cell antigen associated with protective immunity against tuberculosis.

L19 ANSWER 4 OF 18 MEDLINE on STN
1998437175. PubMed ID: 9761766. Identification and characterization of high molecular-mass mucin-like glycoproteins in the plasma membrane of airway epithelial cells. Paul E; Lee D I; Hyun S W; Gendler S; Kim K C. (Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, Maryland, USA. ) American journal of respiratory cell and molecular biology, (1998 Oct) Vol. 19, No. 4, pp. 681-90. Journal code: 8917225. ISSN: 1044-1549. Pub. country: United States. Language: English.
AB A previous lectin binding study demonstrated the presence of high molecular-mass mucin-like glycoproteins (HMGP) on the surface of hamster tracheal surface epithelial (HTSE) secretory cells (Proc. Natl. Acad. Sci. USA 1987;84:9304). In the present study, we intended to isolate and characterize these HMGP from the plasma membrane of the primary HTSE cells and then to determine whether or not these membrane HMGP are Muc-1 mucins, a type of mucins originally discovered on the surface of some carcinomas. A subcellular fraction enriched with the plasma membrane was obtained using a sucrose density gradient centrifugation. This fraction contained high molecular-mass glycoconjugates which were excluded from Sepharose CL-4B gel. Biochemical characterization of these glycoconjugates revealed the following characteristics: (1) susceptibility to both pronase and mild alkaline treatments, but totally resistant to proteoglycan-digesting enzymes; (2) partitioning in the detergent phase of Triton X-114 and resistance to digestion by phosphatidylinositol phospholipase C or D; (3) a buoyant density of 1.5 g/ml based on CsCl density gradient centrifugation; (4) polydispersity in terms of both size and charge density; and (5) lack of immunoreactivity with an anti-Muc-1 mucin antibody. We conclude that the plasma membrane of HTSE cells at confluence contains HMGP, which seem to be the integral membrane proteins but different from Muc-1 mucins, and that these membrane HMGP appear to share some similarities with secreted mucins in terms of size and charge.

L19 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2005:611827 Document No. 143:133228 Methods for the synthesis of nucleic

acid carrier compositions. Kosak, Kenneth M. (USA). U.S. Pat. Appl. Publ. US 20050153913 A1 20050714, 38 pp., Cont.-in-part of U.S. Ser. No. 829,551. (English). CODEN: USXXCO. APPLICATION: US 2004-878175 20040628. PRIORITY: US 2001-829551 20010410.

AB This invention discloses compns. and methods for preparing pharmaceutical nucleic acid carriers. The compns. comprise a carrier substance coupled to a nucleic acid intercalator whereby the intercalator is coupled by intercalation to the nucleic acid. The compns. can also include a biocleavable linkage for carrying and releasing nucleic acids for therapeutic or other medical uses. The invention also discloses nucleic acid carrier compns. that are coupled to targeting mols. for targeting the delivery of nucleic acids to their site of action.

L19 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334233P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan, mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L19 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

2004:589223 Document No. 141:122414 Methods for glycan remodeling and glycoPEGylation of therapeutic proteins. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040142856 A1 20040722, 690 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410913 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-438582P 20030106; US 2003-360779 20030219; US 2003-448381P 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Thus, polyethylene glycols were conjugated to CMP or UDP nucleosides for use in modifying recombinant therapeutic proteins.

L19 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2004:533807 Document No. 141:87907 Methods for glycan remodeling and glycoPEGylation of therapeutic proteins. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040126838 A1 20040701, 754 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410997 20030409. PRIORITY: US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Thus, polyethylene glycols were conjugated to CMP or UDP nucleosides for use in modifying recombinant therapeutic proteins.

L19 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2004:333839 Document No. 140:352406 Erythropoietin glycosylation and the modification of protein structure and activity for therapeutic use. De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2004033651 A2 20040422, 1018 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US31974 20031008. PRIORITY: WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219; US 2003-410945 20030409.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Methods of modifying the structure and properties of erythropoietin by introduction of glycosidation are described. The method uses substitution variants of erythropoietin to introduce sites that can be glycosylated enzymically. The primary glycosylation may then be used to add further sugar residues. The glycosidation, which may include the introduction of N-acetylglucose, N-acetylgalactose, and sialic acid and mannosyl and fucosyl oligosaccharides. The carbohydrate moiety may in turn be modified by PEGylation. A biantennary glycosidated derivative of Epogen had 146% of the activity of the unmodified protein. The glycosylated proteins had longer serum half-lives than the unmodified protein and showed longer term effects on blood Hb levels.

L19 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a

peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

L19 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2003:532329 Document No. 139:106453 p-Amidobenzyl ethers of drugs in drug delivery systems. Senter, Peter D.; Toki, Brian E. (USA). U.S. Pat. Appl. Publ. US 20030130189 A1 20030710, 43 pp., Cont.-in-part of U.S. Ser. No. 963,103. (English). CODEN: USXXCO. APPLICATION: US 2002-252947 20020923. PRIORITY: US 2001-963103 20010924.
AB Compns. containing conjugates containing a drug moiety, a ligand and an optional acyl unit, an amino acid or a peptide, an aminobenzyl ether self-immolative spacer group, an optional second self-immolative group, and carriers, diluents and/or excipients, and methods of delivery the drug are described. Thus, a peptide was treated with 1-naphthol to give a derivative The compound was very stable in human serum, and showed antitumor activity.

L19 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2003:301098 Document No. 138:316492 Glycan remodeling and glycoconjugation of peptides and proteins. De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2003031464 A2 20030417, 900 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US32263 20021009. PRIORITY: US 2001-344692P 20011019; US 2001-334233P 20011128; US 2001-334301P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717;

US 2002-404249P 20020816; US 2002-407527P 20020828.

AB The invention includes methods and compns. for the cell-free in vitro addition and/or deletion of sugars to or from a peptide mol. in such a manner as to provide a glycopeptide mol. having a specific customized or desired glycosylation pattern, wherein the glycopeptide is produced at an industrial scale. The glycopeptide so produced may have attached thereto a modified sugar that has been added to the peptide via an enzymic reaction. A key feature of the invention is to take a peptide produced by an cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a glycopeptide having a glycosylation pattern suitable for therapeutic use in a mammal. More specifically, it is possible to prepare a glycopeptide mol. having a modified sugar mol. or other compound conjugated thereto, such that the conjugated mol. confers a beneficial property on the peptide. The conjugate mol. is added to the peptide enzymically because enzyme-based addition of conjugate mols. to peptides has the advantage of regioselectivity and stereoselectivity. It is therefore possible to remodel a peptide by confering upon the peptide a desired glycan structure preferably having a modified sugar attached thereto, and to generate the glycopeptides at an industrial scale. The invention thus provides a practical solution for the efficient production of improved therapeutic peptides.

L19 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

2003:42137 Document No. 138:95563 Products for treating ovarian cancers and for preventing relapses. Poulain, Laurent; Staedel, Cathy; Gauduchon, Pascal; Erbacher, Patrick; Behr, Jean-Paul (Centre Regional de Lutte Contre le Cancer - Centre Francois Baclesse, Fr.; Institute National Sante Research Medicine). PCT Int. Appl. WO 2003004064 A2 20030116, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (French). CODEN: PIXXD2. APPLICATION: WO 2002-FR2350 20020704. PRIORITY: FR 2001-8864 20010704.

AB The invention relates to products for treating ovarian cancers and for preventing relapses. Said products contain (1) a non-viral nucleic acid vector comprising at least one polyethyleneimine or a derivative thereof, (2) a nucleic acid sequence comprising the gene bcl-xS or a functional fragment thereof and (3) at least one anti-tumoral agent which is active against ovarian cancer, as a combined preparation for sequential use in the treatment of ovarian cancer, the sequence of nucleic acid associated with said non-viral nucleic acid vector being administered after the anti-tumoral compound

L19 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

2001:747650 Document No. 135:293987 Camptothecin conjugates as proliferation inhibitors. Wrenn, Simeon M.; Rubinfeld, Joseph (Supergen, Inc., USA). PCT Int. Appl. WO 2001074402 A2 20011011, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US6855 20010302. PRIORITY: US 2000-540859 20000331.

AB A compound that includes a camptothecin conjugated to a lactone ring protecting moiety, the kits including the compound, and methods of making

and using the compound for cell proliferation inhibition are described. For example, 9-nitrocamptothecin (9NC) was reacted with phosgene and the resulting product was purified. The PEG phosphate diester conjugate was formed using the polyethylene glycol, averaging 100,000 mol. weight, and the 9NC phosgene product. The resulting compound was purified and used to prepare a coated stent. The stent was then deployed at the lesion site of a pig artery using a conventional stent deployment catheter and balloon. After one week, the pig was sacrificed, and the degree of restenotic growth was determined This amount of growth was compared against a control animal where the deployed stent was not coated.

L19 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2001:391990 Document No. 135:16019 Asymmetric hammerhead ribozymes and their diagnostic and therapeutic use. Hendry, Philip; McCall, Maxine J. (Commonwealth Scientific Industrial Research Organization, Australia). U.S. US 6238917 B1 20010529, 30 pp., Cont.-in-part of U.S. Ser. No. 627,033, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1998-156828 19980918. PRIORITY: US 1996-627033 19960402; WO 1997-AU210 19970402.

AB Hammerhead ribozymes that have an asym. loop structure and that have higher than normal cleavage rates are described for use in the control of gene expression by cleavage of a transcript. The ribozyme may be covalently linked to a delivery agent. The invention also includes a composition which comprises the compound in association with an acceptable carrier.

The invention also includes a method of cleaving an RNA target sequence which comprises contacting a target sequence with the compound as described above. Further, a method of treating a disease in man or animals associated with a particular RNA which comprises administrating to the man or animal the compound Further, the invention also includes a diagnostic reagent which comprises the compound Asym. hammerhead ribozymes acting on rat growth hormone mRNA, the Drosophila melanogaster Kruppel gene mRNA, and the HIV-1 tat gene were used to determine the contributions of the loops of the hammerhead ribozyme to the catalytic activity of the ribozyme and sequence requirements were characterized and optimized.

L19 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2001:167842 Document No. 134:236232 New interferon β-like molecules. Pedersen, Anders Hjelholt; Schambye, Hans Thalsgaard; Andersen, Kim Vilbour; Bornaes, Claus; Rasmussen, Poul Baad (Maxygen APS, Den.). PCT Int. Appl. WO 2001015736 A2 20010308, 108 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-DK471 20000825. PRIORITY: DK 1999-1197 19990827; US 1999-PV160782 19991021; DK 1999-1691 19991126; DK 2000-194 20000207; DK 2000-363 20000307; DK 2000-642 20000414.

AB A conjugate exhibiting interferon β activity comprises at least one first non-polypeptide moiety covalently attached to an interferon β polypeptide, the amino acid sequence of which differs from that of wild-type human interferon β in at least one introduced and at least one removed amino acid residue comprising an attachment group for said first non-polypeptide moiety. The first non-polypeptide moiety is, e.g., a polymer mol. or a sugar moiety. The conjugate finds particular use in therapy.

L19 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN
2000:723063 Document No. 133:261528 Use of extended-molecular weight hirudin

as anticoagulant during artificial kidney therapy. Nowak, Gotz; Bucha, Elke (Max-Planck-Gesellschaft zur Forderung der Wissenschaften E.V., Germany). Ger. Offen. DE 19915862 A1 20001012, 6 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1999-19915862 19990408.

AB Extended-mol.-weight hirudins are disclosed for the preparation of non-autoimmune disease-inducing, non-autoantibody-crossreacting anticoagulants for artificial kidney therapy. In particular, no type II thrombocytopenia is caused, and no crossreactivity with antibodies against platelet factor 4-heparin-complex is seen. The extended-mol.-weight hirudins of the invention include e.g. hirudin conjugated with polyethylene glycol.

L19 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2008 ACS on STN

2000:307077 Document No. 132:320935 Induction of humoral anergy using immunogen conjugates lacking T-cell epitopes. Coutts, Stephen M.; Barstad, Paul A.; Iverson, G. Michael; Jones, David S. (La Jolla Pharmaceutical Company, USA). U.S. US 6060056 A 20000509, 30 pp., Cont.-in-part of U.S. 5,268,454. (English). CODEN: USXXAM. APPLICATION: US 1993-118055 19930908. PRIORITY: US 1991-652648 19910208.

AB The authors disclose the preparation of conjugates of non-immunogenic carrier mols. with B-cell epitopes that possess ability to suppress antigen-specific antibody responses. In one example, mice were primed with the main immunogenic region of the acetylcholine receptor. Subsequent immunization of these mice with a B-cell epitope peptide, lacking the ability to activate primed T-cells, led to a specific suppression of the anti-receptor antibody response. In a second example, mice were primed with the bee venom allergen, mellitin. Immunization with peptides conjugated to lysine-glutamate copolymer suppressed the anti-mellitin response.

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L21        445 L20 AND CONJUGATE

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L22        124 L21 AND ANTIBOD?

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L24 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN

2008:91238 Document No. 148:186600 Glycosylation and PEGylation of polypeptides via engineered O-linked glycosylation sequences and pharmaceutical applications. DeFrees, Shawn (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2008011633 A2 20080124, 254pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE,

IS, IT, LU, MC, ML, MR, MT, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2007-US74139 20070723. PRIORITY: US 2006-832461P 20060721; US 2007-881130P 20070118; US 2007-886616P 20070125; US 2007-941920P 20070604.

AB The present invention relates to a method of preparing glycosylated polypeptides using short enzyme-recognized O-linked or S-linked glycosylation sequences. The present invention provides sequon polypeptides with an amino acid sequence including one or more exogenous O-linked glycosylation sequence of the invention. In addition, the present invention provides methods of making polypeptide conjugates (e.g., PEGylation) as well as methods of using such conjugates and their pharmaceutical compns. The invention further provides libraries of sequon polypeptides, wherein each member of such library includes at least one exogenous O-linked glycosylation sequence of the invention. Also provided are methods of making and using such libraries. Exemplary incorporation of glycosylation sites into human BMP-7, FGF-21 and neurotrophin-3 and their expression using various vectors and E. coli host cells is described.

L24 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN

2007:269736 Document No. 146:414546 Improvement of a Recombinant Anti-Monkey Anti-CD3 Diphtheria Toxin Based Immunotoxin by Yeast Display Affinity Maturation of the scFv. Wang, Zhirui; Kim, Geun-Bae; Woo, Jung-Hee; Liu, Yuan Yi; Mathias, Askale; Stavrou, Scott; Neville, David M., Jr. (Section on Biophysical Chemistry, Laboratory of Molecular Biology, National Institute of Mental Health, Bethesda, MD, 20892-1216, USA). Bioconjugate Chemistry, 18(3), 947-955 (English) 2007. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB Recently, a bivalent recombinant antihuman CD3 diphtheria toxin (DT) based immunotoxin derived from the scFv of UCHT1 antibody has been made that shows enhanced bioactivity and is free from the side effects of Fc receptor interaction. In this case, the diminution of CD3 binding due to the placement of the scFv domain at the C-terminus of the truncated DT in single scFv immunotoxins was compensated by adding an addnl. scFv domain. However, this strategy was less successful for constructing an antirhesus recombinant immunotoxin derived from the scFv of FN18 antibody due to poor binding of the antirhesus bivalent immunotoxin. The authors report here that, by increasing the FN18 scFv affinity through random mutagenesis and selection with a dye-labeled monkey CD3εγ recombinant heterodimer, the authors greatly improved the bioactivity of FN18 derived immunotoxin. The best mutant, C207, contained nine mutations, two of which were located in CDRs that changed the charge from neg. to pos. Binding affinity of the C207 scFv to the monkey T cell line HSC-F increased 9.8-fold. The potency of the C207 bivalent immunotoxin assayed by inhibition of protein synthesis increased by 238-fold.

L24 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN

2007:1353067 Document No. 148:31157 A fold-back single-chain diabody format enhances the bioactivity of an anti-monkey CD3 recombinant diphtheria toxin-based immunotoxin. Kim, Geun-Bae; Wang, Zhirui; Liu, Yuan Yi; Stavrou, Scott; Mathias, Askale; Goodwin, K. Jeanine; Thomas, Judith M.; Neville, David M. (Section on Biophysical Chemistry, Laboratory of Molecular Biology, National Institute of Mental Health, Bethesda, MD, 20892-1216, USA). Protein Engineering, Design & Selection, 20(9), 425-432 (English) 2007. CODEN: PEDSBR. ISSN: 1741-0126. Publisher: Oxford University Press.

AB T-cell depleting anti-CD3 immunotoxins have utility in non-human primate models of transplantation tolerance and autoimmune disease therapy. We recently reported that an affinity matured single-chain (scFv) anti-monkey CD3 antibody, C207, had increased binding to T-cells and increased bioactivity in a diphtheria toxin (DT)-based biscFv

immunotoxin compared with the parental anti-body, FN18. However, FN18 scFvs and their mutant derivs. such as C207 did not exhibit robust bivalent character in the biscFv format. We now report that C207 in a diabody format exhibits a 7-fold increase in binding to T-cells over scFv (C207) indicating considerable divalent character for the diabody. This construct was formed by reducing the VL/VH linker to five residues and was secreted from Pichia pastoris as the non-covalent dimer. An immunotoxin based on this diabody format was secreted as a non-covalent dimer but was devoid of bioactivity and failed to bind T-cells, suggesting steric hindrance from the two large closely positioned truncated DT moieties. We constructed a single-chain diabody immunotoxin by fusing to the truncated DT C-terminus L1-VL-L1-VH-L2-VL-L1-VH where L1 is a five-residue linker and L2 is the longer (G4S)3 linker permitting interactions between the distal and proximal VL/VH domains. This 'fold-back' immunotoxin was secreted predominantly as the monomer and exhibited a 5- to 7-fold increase in bioactivity over DT390biscFv(C207) and depleted monkey T-cells in vivo.

L24 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
2008:143676 The development and optimization of ELISA for the determination of tetrodotoxin. Zhou, Yu; Li, Yan-song; Pan, Feng-guang; Liu, Zeng-shan; Wang, Zhe (Key Laboratory of Zoonoses, Ministry of Education, Insitute of Zoonoses, Jilin University, Changchun, 130062, Peop. Rep. China). Journal of Medical Colleges of PLA, 22(6), 347-351 (English) 2007. CODEN: JMCPE6. ISSN: 1000-1948. Publisher: Journal of Medical Colleges of PLA, Editorial Board.
AB Objective: To optimize the ELISA for the determination of tetrodotoxin. Methods:
A competitive ELISA (ELISA) was used. In the ELISA, 100 μl antigen (1.0 μg/mL) was coated on the microtiter plate for 60 min at 37°C or over night at 4°C. The plate was then washed 3 times with PBS-T for 3-5 s each time. The optimal incubation time for monoclonal antibody (mAb), goat anti-mice IgG peroxidase conjugate and OPD were 30 min, 20 min and 10 min at 37°C, resp. Results: The detection limit is 0.05 ng in each well. The curve was linear for TTX doses between 5-5 000 ng/mL (0.25-250 ng for every assay). The linear regress equation was Y = 0.30 88X-0.17 41 (R = 0.99 01). The average callback for TTX of muscles and gonads were 99.74% and 100.30%, resp. The sensitivity of optimization ELISA was 5 times than traditional method and the time of 1.8 h were saved. Conclusion: The optimized ELISA is an ideal method for the determination of tetrodotoxin.

L24 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
2005:121065 Document No. 142:204915 Antibody-toxin conjugates. Defrees, Shawn; Wang, Zhi-Guang (Neose Technologies, Inc., USA). PCT Int. Appl. WO 2005012484 A2 20050210, 126 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US24042 20040726. PRIORITY: US 2003-490168P 20030725; US 2003-499448P 20030902.
AB In response to the need for improved site-specific delivery of toxins to the loci of disease, the present invention provides antibodies that are modified with toxins. The invention provides a unique class of conjugates in which the toxin is attached to the antibody through a glycosyl linking group, e.g., an intact glycosyl linking group, which is attached to the peptide

(or to an acceptor moiety attached to the peptide, e.g. a spacer or amplifier) utilizing an enzymically-mediated coupling reaction. Thus, in a first aspect, the present invention provides a peptide conjugate in which the sugar-toxin construct (modified sugar) is attached to a peptide. For example, the invention provides a peptide conjugate having the formula: Ab-G-L-T wherein Ab is an antibody, or other targeting moiety; G is a glycosyl linking group, e.g., an intact glycosyl linking group, covalently joining Ab to L; L is a bond or a spacer moiety covalently joining G to T; and T is a toxin, or other therapeutic agent. In a second aspect, the invention provides a compound having the formula: S-L-T wherein S is a nucleotide sugar; L is a bond or a spacer moiety covalently joining S to T; and T is a toxin moiety.

L24 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
2005:409140 Document No. 142:487367 Cell-free in vitro glycan remodeling and enzymic glycoconjugation of Factor IX for treating hemophilia B. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050100982 A1 20050512, 761 pp., Cont.-in-part of U. S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410897 20030409. PRIORITY: US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB A method is disclosed for remodeling a peptide, including the addition or deletion, if necessary, of one or more glycosyl groups of the peptide, then enzyme-mediated attachment of a PEGylated sugar. A key feature of the invention is to take a peptide produced by any cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a peptide having a glycosylation pattern suitable for therapeutic use in a mammal. The invention includes a cell-free, in vitro method of remodeling and PEGylation of Factor IX using glycosyltransferase, sialyltransferase and sialidase. Exemplary glycoPEGylation of Factor IX produced in CHO cells, direct sialyl-glycoPEGylation of Factor IX, and sialic acid capping of glycoPEGylated Factor IX are described. Other proteins were glycoPEGylated in a similar manner. The Factor IX of the invention is used for treating hemophilia B in human.

L24 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
2005:122585 Document No. 142:217398 Cell-free in vitro glycoconjugation of interleukin 2 as therapeutic agent against cancer and AIDS in mammal and human. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20050031584 A1 20050210, 750 pp., Cont.-in-part of U.S. Ser. No. 360,779. (English). CODEN: USXXCO. APPLICATION: US 2003-410980 20030409. PRIORITY: US 2001-328523P 20011010; US 2001-344692P 20011019; US 2001-334301P 20011128; US 2001-334233P 20011128; US 2002-387292P 20020607; US 2002-391777P 20020625; US 2002-396594P 20020717; US 2002-404249P 20020816; US 2002-407527P 20020828; WO 2002-US32263 20021009; US 2002-287994 20021105; US 2003-360770 20030106; US 2003-360779 20030219.
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The method uses enzyme to remove or add phosphate, sulfate, carboxylate and/or ester group-containing saccharide to interleukin 2 peptide, and then conjugate the saccharide-linked interleukin 2 with modifying group such as polymer, therapeutic moiety, detectable label, toxin, radioisotope, targeting moiety and peptide. The saccharide group comprises monosaccharyl, oligosaccharyl, glycosyl, truncated glycan,

mannosyl, GlcNAc, xylosyl, sialyl, galactosyl, glucosyl or GalNAc. The enzyme for the saccharide addition or removal is a prokaryotic or eukaryotic glycosyltransferase selected from sialyltransferase, galactosyltransferase, glucosyltransferase, GalNAc transferase, GlcNAc transferase, fucosyltransferase, mannosyltransferase, endo-N-acetylgalactosaminidase, glycosidase, sialidase, mannosidase, etc. The substrate is a nucleotide sugar such as UDP-glucose, UDP-galactose, UDP-galactosamine, UDP-glucosamine, UDP-N-acetylgalactosamine, UDP-N-acetylglucosamine, GDP-mannose, GDP-fucose, CMP-sialic acid and CMP-NeuAc.

L24 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2008 ACS on STN
2004:182383 Document No. 140:231203 Methods for cell-free remodeling and glycoconjugation of glycopeptides, remodeling of α-galactosidase A peptides, and their therapeutic use for Fabry disease. Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi (Neose Technologies, Inc., USA). U.S. Pat. Appl. Publ. US 20040043446 A1 20040304, 761 pp., Cont.-in-part of Appl. No. PCT/US02/32263. (English). CODEN: USXXCO. APPLICATION: US 2003-411037 20030409. PRIORITY: US 2002-2002/PV38729U 20020607; US 2002-2002/PV39177U 20020625; US 2002-2002/PV39659U 20020717; US 2002-2002/PV40424U 20020816; US 2002-2002/PV40752W 20020828; WO 2002-US32263 20021009.
AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. The invention claims a method of remodeling an α-galactosidase A peptide in vitro by removing a saccharyl subunit from the peptide and contacting the truncated glycan with at least one glycosyltransferase and a glycosyl donor to transfer the glycosyl donor to the glycan moiety. The glycosyl donor may contain a modifying group such as a polymer, a therapeutic toxin, a detectable label, a reactive linker group, or a targeting mol. The invention specifically claims α-galactosidase glycopeptides containing mannooligosaccharide or sialyloligosaccharide structures and their modification with a galactosyltransferase, a sialyltransferase, or a mannosyltransferase and modified glycosyl donors such as UDP-Gal-polyethylene glycol (PEG)-transferrin , CMP-sialic acid linker-mannose-6-phosphate, CMP-sialic acid-PEG, or GDP-mannose-linker-ApoE. Conjugation of glycopeptides with PEG, for example, is intended to reduce the immunogenicity of peptides and prolong their half-life in circulation. Conjugation of glycopeptides with transferrin is intended to transport glycoconjugates across the blood-brain barrier. In addition, the invention claims therapeutic use of a glycoconjugated α-galactosidase A peptide for Fabry disease. Examples of the invention include synthesis of CMP-sialic acid, UDP-galactose, UDP-glucosamine, and UDP-galactosamine conjugates with polyethylene glycol, sialylation of recombinant glycoproteins antithrombin III, fetuin, and α1-antitrypsin by recombinant rat ST3Gal III, and glyco-remodeling of Cri-IgG1 monoclonal antibody. The general procedure for making UDP-GlcNAc-PEG is that the protected amino sugar diphospho-nucleotide is oxidized to form an aldehyde at the 6-position of the sugar. The aldehyde is converted to the corresponding primary amine by formation and reduction of the Schiff base. The resulting intermediate is contacted with the p-nitrophenol carbonate of m-PEG, which reacts with the amine, binding the m-PEG to the saccharide via an amide bond.

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